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When magnetic resonance imaging is needed: malignant pleural mesothelioma with transdiaphragmatic infiltration and localized appearance: a case report

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Abstract: Malignant pleural mesothelioma (MPM) most commonly presents with diffuse growth pattern and wide-spread infiltration of the pleural surface. In rare cases, also a localized form with a circumscribed pleural tumor mass has been identified. We report a case of MPM presenting with an atypical, radiologically localized appearance which was later proven to be a disseminated disease. After staging by positron-emission computed tomography (PET-CT), magnetic resonance imaging (MRI) was primarily used for planning the surgical resection. To date, no clinical evidence is available on the role of MRI for preoperative planning of the surgical approach. In a 58-year-old woman, CT revealed a solitary tumor bulk on the left diaphragm and transdiaphragmatic infiltration. Although CT in general is the method of choice to assess the tumor extent, this case clearly highlights the value of contrast MRI for assessing the diaphragmatic and soft tissue infiltration. Surgical resection was preformed and the intraoperative examination and frozen section revealed a disseminated pleural spread, corresponding to a diffuse pleural mesothelioma. The patient made an uneventful recovery and the radiological follow-up 1 year after surgery showed no signs of relapse. This case demonstrates that diffuse pleural mesothelioma may mimic imaging-wise a localized variant and highlights the importance of thorough preoperative assessment using MRI and intraoperative examination of the pleural cavity in these patients.

Keywords: Malignant pleural mesothelioma (MPM); magnetic resonance imaging (MRI); extended pleurectomy; decortication; multimodality treatment; case report

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Introduction

Malignant pleural mesothelioma (MPM) is an aggressive tumor of the mesothelial lining of the chest and is most commonly associated with an occupational exposure to asbestos (1). In most cases, MPM shows a diffuse growth pattern and spreads widely across the pleural surface (2). However, sporadic cases of localized MPM with a bulky, circumscribed appearance have been initially described over 40 years ago (3). While both, localized and diffuse MPM, display identical histological, immunohistochemical and molecular characteristics, localized MPM mostly show a less aggressive clinical course and the role of chemotherapy after localized surgical resection remains controversial (4-7). In order to differentiate between a localized MPM and the rare variant of a diffuse MPM with a dominant, circumscribed mass, a complete examination of the pleural cavity is required (5).

Computed tomography (CT) in general is the standard of reference for primary assessment of tumor extend. For tumor staging ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission computed tomography (PET-CT) is used. However, there are different studies showing that magnetic resonance tomography (MRI) goes beyond CT concerning the depiction of diaphragmatic and chest wall infiltration.

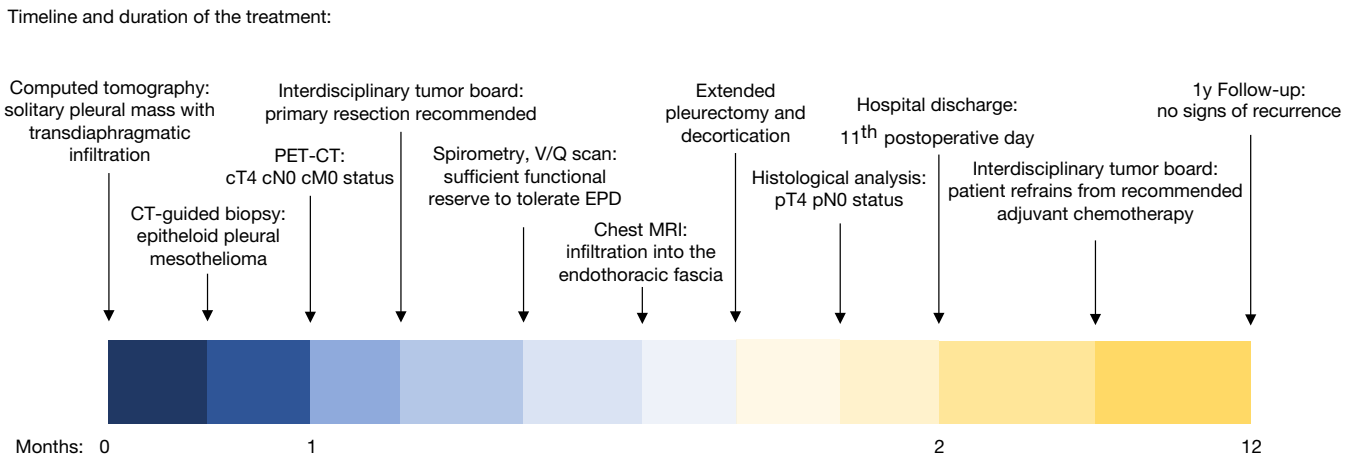

Figure 1 Timeline and duration of the diagnostic and therapeutic interventions, including the follow-up period up to date. CT, computed tomography; MRI, magnetic resonance tomography; PET, positron emission tomography; V/Q-scan, ventilation-perfusion scan.

Here, we report the rare case of a diffuse MPM with radiologically localized appearance and transdiaphragmatic infiltration. The atypical presentation featuring a solitary tumor bulk and the subsequent histological confirmation of a disseminated disease add to the educational value of this case. In addition, the surgical planning was primarily performed according to the findings of the preoperative MRI. The role of MRI for preoperative planning has not been previously described and clinical evidence is therefore poor. For the review of clinical records and the publication of this case, an informed consent was obtained from the patient. A timeline of each diagnostic or therapeutic intervention is depicted in *Figure 1*. We present the following article/case in accordance with the CARE guideline checklist (available at http://dx.doi.org/10.21037/ccts-20-41).

Case presentation

A 58-year-old female patient from east Asia presented with a recent onset of postprandial gastric discomfort, night sweats and weight loss. While both gastroscopy and colonoscopy showed not pathological findings, a CT revealed a solitary, partly solid and partly cystic pleural mass, measuring 9.4 cm × 5.8 cm. The tumor was located on the left diaphragm with transdiaphragmal infiltration and slight displacement of the stomach, the spleen and the liver (*Figure 2*). No pleural or peritoneal effusion was present. Upon CT-guided transthoracic biopsy, a MPM with epithelioid differentiation was diagnosed. Immunohistochemistry showed a positivity for CK5/6, CK7 and WT1. In the immunostaining for BAP-1 no retained expression was identified. The patient had no suggestive occupational history of exposure to asbestos. Following further staging by PET-CT, no other pleural or abdominal lesions and no mediastinal lymphadenopathy were identified and a clinical T4 N0 M0 status was defined. The mesothelioma showed a ^{18}F-FDG accumulation with maximum standardized uptake value (SUV_{max}) of 15.2. The calculated total tumor volume was estimated at 250 mL. Due to the localized finding without signs of diffuse pleural dissemination or other distant manifestations, a direct resection was recommended in our interdisciplinary tumor board. Pre-operative spirometry showed sufficient functional reserve [FEV1: 1.86L (84% of set)] and the perfusion of the diseased left lung (V/Q-scan) was only moderately reduced at 37%. For preoperative planning a MRI of the chest was performed, showing the transdiaphragmatic growth and infiltration into chest wall (*Figures 2*,*3*,*4*). The tumor showed a moderate contrast-uptake but a high signal on diffusion-weighted image, which is typical for epitheleoid mesothelioma. Furthermore, the MR showed an infiltration into the fascia endothoracica of the chest wall (*Figure 4*).

The patient underwent an extended pleurectomy and decortication with resection of pericardium and diaphragm, followed by a systematic lymphadenectomy of the mediastinal lymph nodes (Supplementary file). The pericardium was reconstructed with an acellular biological patch. After resection of the diaphragm encompassing the bulky tumor, the peritoneal cavity was opened and

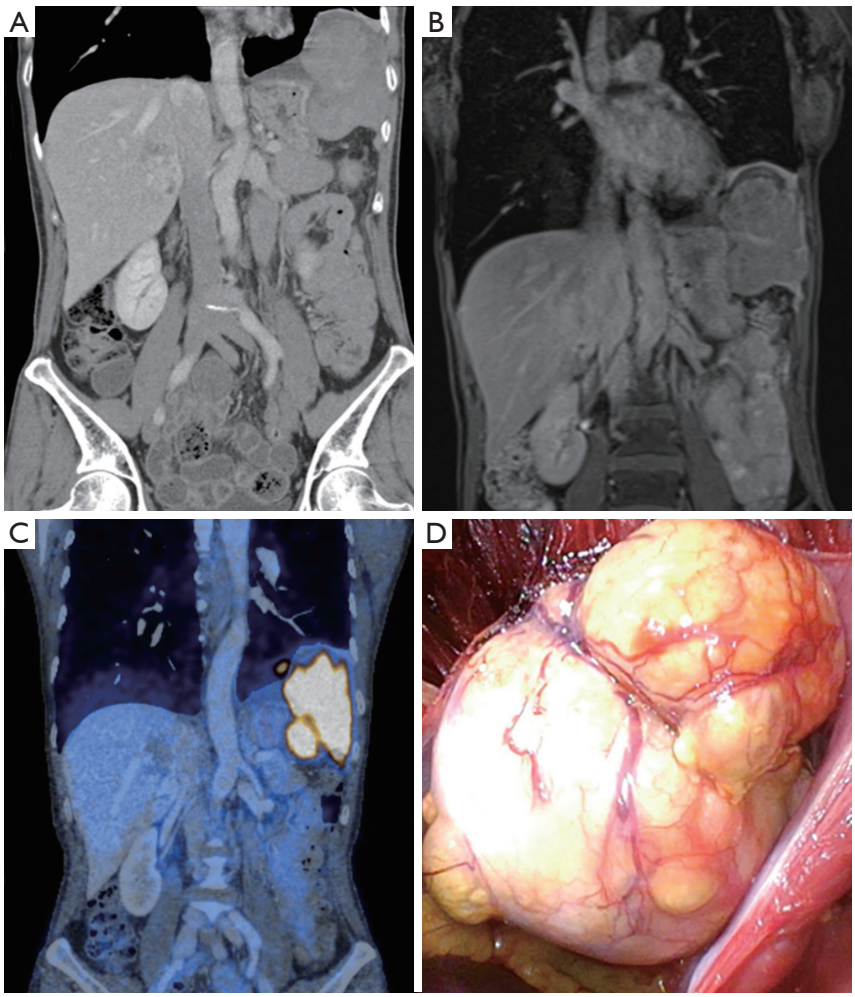

Figure 2 Pre-operative scans in coronal plane. (A) CT, (B) T1-weighted MRI and (C) ^{18}F-FDG-PET/CT demonstrating focus of left-sided MPM with transdiaphragmatic infiltration and slight displacement of the stomach, the spleen and the liver. (D) Intraoperative view of the resected bulky tumor (9.4 cm × 5.8 cm).

inspected. Apart from minor adhesions of the tumor bulk to the greater omentum, no infiltration into the visceral organs was seen macroscopically. The adhesive region of the omentum was resected and the diaphragm was reconstructed with a Gore-Tex® Dualmesh® biomaterial patch (W.L. Gore & Associates Inc., Flagstaff, AZ, USA). Single wedge-resections were necessary in two sites where an infiltration into the lung parenchyma was suspected. While the histological analysis of the partially resected greater omentum confirmed no malignant process, infiltrations of the epithelioid pleural mesothelioma were verified in the specimens of both visceral- and parietal pleura, pericardium and lung parenchyma, corresponding to a pathological T4 N0 M0 status.

The patient was discharged after an uneventful recovery on the 11th postoperative day. Within the intended multimodality treatment approach, an adjuvant chemotherapy with platinum and pemetrexed was planned. However, the patient wished to refrain from chemotherapy. To date, regular clinical and radiological follow-up 1 year after surgery shows no signs of relapse.

Comment

Our case demonstrates a diffuse MPM with a dominant mass on the left hemidiaphragm and transdiaphragmatic infiltration. The radiological findings were at first not suggestive for an MPM and differential diagnoses included

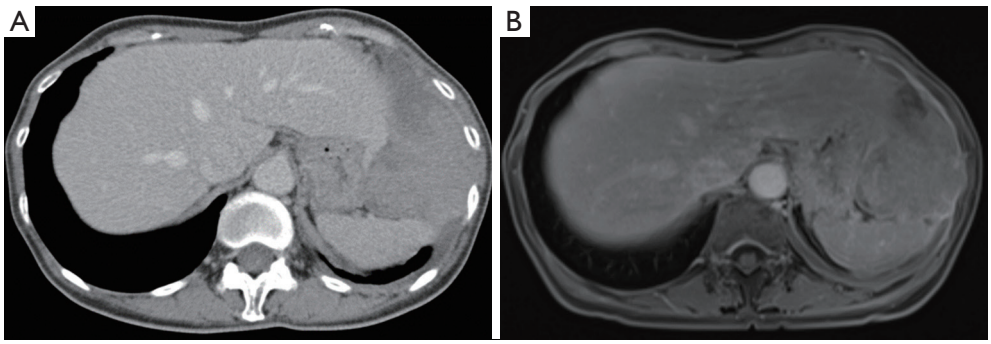

Figure 3 Comparison of contrast-enhanced computed tomography and T1-weighted magnetic resonance imaging in respect to soft tissue resolution and identification of chest wall infiltration. (A) Axial view of the left-sided MPM on contrast enhanced computed tomography of the chest; (B) T1-weighted magnetic resonance imaging with better soft tissue contrast and therefore providing more details on chest wall and diaphragm invasion.

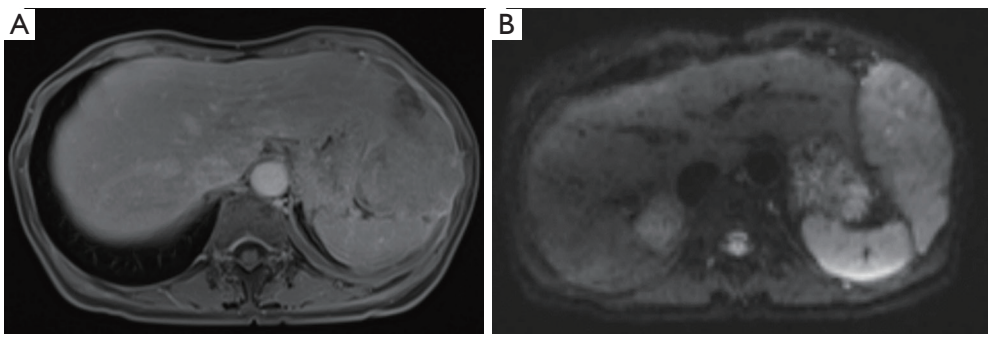

Figure 4 The different roles of T1-weighted and diffusion-weighted magnetic resonance imaging in MPM. (A) Axial T1-weighted MRI showing soft tissue infiltration of the MPM; (B) diffusion-weighted MR imaging (DWI) demonstrating excellent differentiation of malignant pleural disease (white lighted area) from benign pleural alterations.

lymphoma, gastrointestinal stromal tumor or mesenchymal tumors. After histological confirmation of an epithelioid pleural malignancy, a localized MPM was suspected and the patient was therefore referred directly for operative resection, without neoadjuvant chemotherapy, our usual concept of MPM treatment. The intraoperative examination of the complete pleural cavity unfortunately revealed additional nodular lesions on the pericardium, the parietal and the visceral pleura, corresponding to a disseminated disease. Consequently, an adjuvant chemotherapy with platinum and pemetrexed was recommended by our interdisciplinary tumor board.

Localized MPM are assumed to account for approximately 0.5% of all MPM cases (5). Histologically and immunohistochemically, localized MPM are indistinguishable from diffuse MPM (4,5). In a recent study by Hung *et al.*, localized MPM was furthermore found to harbor similar genomic alterations such as BAP1 mutations, deletions in CDKN2A and NF2, TRAF7-mutations and genomic near-haploidization (5). Contrary to diffuse MPM, the association with asbestos exposure and male sex is not as strong and the clinical course is often less aggressive (4). In the largest case series to date by Allen *et al.*, 48% of all patients with localized MPM undergoing isolated surgical resection were free from recurrence after a mean follow-up of 4.8 years (4). Hence, an aggressive treatment and surgical excision is recommended. However, the role of chemotherapy has yet to be assessed in these patients (5-7). In contrast, international guidelines are established for the initial treatment of diffuse MPM and a multimodality concept including (neo)- or adjuvant chemotherapy with platinum and anti-folate doublet, followed by macroscopic complete resection has been shown to extend the overall- and disease-free survival (8-13).

Regarding imaging assessment, chest X-ray is usually the first-line diagnostic approach of MPM showing suspicious unilateral pleural effusion, unilateral pleural thickening with or without thickening pleural fissures, multiple masses with peripheral distribution or loss of volume in the involved hemithorax (14). Contrast enhanced CT of the chest represents the gold standard to evaluate MPM associated features like circumferential pleural thickening (pleural rind), thickened mediastinal pleura, nodular or irregular pleural thickening, infiltration of chest wall, diaphragm, mediastinum or pericardium and lymph nodes in extra pleural fat tissue (15). Although MRI is not routinely performed in patients with MPM, it has excellent soft tissue contrast and is therefore superior to CT for assessing chest wall and diaphragm invasion and revealing endothoracic fascia involvement (*Figure 3*) (16). Furthermore, recent studies have shown promising benefits of diffusion-weighted MR imaging (DWI) to differentiate malignant pleural disease from benign pleural alterations (*Figure 4*) (17) and delayed phase enhancement MRI and early contrast-enhancement MRI are on the verge of significantly improve the accuracy of early diagnosis as well as staging and therapy response assessment of MPM (18,19). Meanwhile, ^{18}F-FDG-PET/CT surpasses CT and MRI in N and M staging of MPM (but not for T-staging) and is beneficial for evaluating treatment response and detection of recurrent disease (20).

While diffuse MPM most commonly presents as a uniform thickening of the pleura, rare cases featuring a circumscribed, bulky lesion may mimic a localized MPM (4,5). Our case report displays that their distinction may be difficult based on the preoperative radiological or bioptic findings. The case therefore highlights the importance of a meticulous intraoperative examination of the pleural cavity in patients where a localized MPM is suspected. The direct comparability between radiological findings from PET-CT and MRI with intraoperative, macroscopic findings and histological, microscopic results substantiate this conclusion in our case. The circumstance that localized pleural mesothelioma forms a rare disease makes it difficult to confirm our findings with other cases. The limitation of this case report are therefore its limited external validity and generalizability.

Conclusions

This case of a localized variant of epithelioid mesothelioma with transdiaphragmatic growth highlights the importance of MRI for a thorough preoperative assessment and of a careful intraoperative examination of the pleural cavity in these patients.

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Footnote

Guideline Checklist: The authors have completed the CARE guideline checklist. Available at http://dx.doi.org/10.21037/ccts-20-41

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ccts-20-41). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Written informed consent was obtained from all patients.

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Discussion

Dr. Hon Chi Suen (Hong Kong, China): The MRI showed infiltration of the endothoracic fascia that CT and PET scan did not show. Did this finding alter the surgical approach and if it did, how?

Dr. Thomas Frauenfelder (Zurich, Switzerland): Dr. Suen raises an important question. In patients with diffuse malignant pleural mesothelioma scheduled for macroscopic complete resection (either by extended pleurectomy and decortication or extrapleural pneumonectomy) after induction chemotherapy, the detection of multilevel chest wall infiltration is most commonly a reason to refrain from radical surgery. In patients where multilevel chest wall infiltration is identified intraoperatively by repeated biopsies and frozen section of suspicious lesions, a parietal pleurectomy without decortication of the visceral pleura is in our opinion a reasonable alternative. We experienced that this approach reduces the duration of postoperative air-leak, while still enabling a de-bulking. In patients where a multilevel chest wall infiltration is preoperatively seen in the MRI, the further treatment plan should be re-discussed at an interdisciplinary tumor board with attending experts in medical oncology, thoracic surgery and radiation oncology.

In our case, the infiltration into the endothoracic fascia was localized to the single tumor bulk and was not considered to be multifocal. We therefore proceeded with the intended resection. However, in patients with unifocal chest wall infiltration we intraoperatively mark the affected area with metal clips in order to facilitate the targeting of a potential adjuvant stereotactic body radiation therapy.

Dr. Suen: The localized main bulk of tumor was transdiaphragmatic. Would you have performed a laparoscopy first to see if there was diffuse peritoneal mesothelioma as well?

Dr. Frauenfelder: This is an excellent remark. Due to the localized appearance of the mesothelioma without radiological signs of further pleural, abdominal or mediastinal lesions, the patient was directly referred for resection of the tumor. With respect to the disseminated disease that was detected intraoperatively, a preceding laparoscopy could have been considered in hindsight.

Dr. Suen: Since initially, it was thought that the tumor was localized to the diaphragm and the plan was to perform a local excision, what was the incision? When it was found that there was actually diffuse malignant pleural mesothelioma, how was the incision modified to accomplish pleurectomy and decortication of the entire left chest?

Dr. Frauenfelder: Dr. Suen addresses a crucial factor of our surgical approach for malignant pleural mesothelioma. For extended pleurectomy and decortication, as well as for extrapleural pneumonectomy we perform an extended lateral thoracotomy and enter the 6th intercostal space. In all cases, the costal arch is ventrally excised for an improved exposure of the situs. This maneuver considerably facilitates the dissection of the costophrenic sinus and resection of the diaphragm. Therefore, no further utility thoracotomy is required.

Since in our case, a local resection and reconstruction of the diaphragm had already been planned, the abovementioned incision was performed in the first place and was well suitable for the subsequent pleurectomy and decortication.